REMARKS

By the present amendment, claims 1, 4, 6, 13, 20, 23, 25, 41, 42 and 44 have been amended and claims 2, 3, 21 and 22 have been deleted. The amendment renders claims 1, 4-20, 23-30 and 41-44 pending in the application. The amendments to the claims have been made without prejudice and without acquiescing to any of the Examiner's objections. Applicant reserves the right pursue any of the deleted subject matter in a further divisional, continuation or continuation-in-part application. No new matter has been entered in this amendment and its entry is respectfully requested.

The Official Action dated August 22, 2002 has been carefully considered. It is believed that the amended claims submitted herewith and the following comments represent a complete response to the Examiner's rejections and place the present application in condition for allowance. Reconsideration is respectfully requested.

35 U.S.C. §112, second paragraph

1. The Examiner has objected to claims 1-30 and 41-44 under 35 U.S.C. §112, second paragraph as being indefinite in view of the recitation of "derived from". In response, these claims have been amended, without prejudice, in order to delete the term "derived".

In view of the foregoing, we respectfully request that the objections to the claims under 35 U.S.C. §112, second paragraph be withdrawn.

35 U.S.C. §112, first paragraph

2. The Examiner has objected to claims 1-26, 28-30 and 41-44 under 35 U.S.C. §112, first paragraph as lacking enablement.

In response, independent claims 1, 20, 41 and 42 have been amended in order to specify that the zymogen is an aspartic protease. Support for this amendment can be found in the application as filed as well as in previous claims 3 and 22 which have been deleted. The application provides sufficient and clear guidance as to how to use an aspartic protease (such as chymosin) in the methods and compositions of the invention. In view of the comparability of the catalytic mechanism of aspartic proteases, undue experimentation would not be required to practice the claims (as amended) especially in view of the presence of working examples and the amount of direction and guidance present in the application.

The Examiner has also objected to the term "pharmaceutical" in claim 41. In response, this term has been deleted from the claim.

In view of the foregoing, we respectfully request that the objections to the claims under 35 U.S.C. §112, first paragraph be withdrawn.

35 U.S.C. §102/103

3. The Examiner has objected to claims 1-7, 9-13, 15-26, 28-30 and 41-44 under 35 U.S.C. §102(a) as being anticipated by or, in the alternative, unpatentable over Moloney (WO 96/21029). We respectfully disagree with the Examiner for the reasons that follow.

As we have previously indicated to the Examiner, the Moloney application teaches a nucleic acid construct comprising a nucleic acid encoding an oil body protein (OBP) linked to a nucleic acid including a heterologous protein. In one embodiment, the heterologous protein can be chymosin which would result in the preparation of a fusion protein as follows: NH3 - Oil Body Protein-Prochymosin-Chymosin-COOH.

In contrast, the claims of the present invention require that the heterologous protein, which would be the oil body protein in the Moloney reference, is located immediately downstream of the nucleic acid sequence encoding the pro-peptide. Therefore, in accordance with the present invention, in the above representation the nucleic acid sequence encoding the chymosin sequence would have to be replaced with a nucleic acid sequence heterologous to the pro-chymosin sequence. Such an embodiment is not taught or suggested in Moloney. Consequently, the claims of the present case are not anticipated by Moloney.

We also submit that Moloney does not provide motivation or suggestion to one of skill in the art to prepare a fusion protein wherein the pro-chymosin sequence is located immediately upstream of the oil body protein sequence. Absent motivation or reasonable expectation of success, Moloney cannot be said to render the present claims obvious.

Applicant was the first to demonstrate that a nucleic acid sequence encoding a pro-sequence of an aspartic protease when linked to a nucleic acid sequence encoding a polypeptide heterologous to the pro-sequence can function as a recognition sequence for the mature form of an autocatalytically maturing zymogen so that the pro-peptide then can be cleaved from the fusion protein to release the heterologous recombinant polypeptide.

In view of the foregoing, we respectfully request that the objections to the claims under 35 U.S.C. §102 or 35 U.S.C §103 in view of Moloney be withdrawn.

35 U.S.C. §103

4. The Examiner has objected to claim 8 under 35 U.S.C. §103(a) as being unpatentable over Moloney (WO 96/21029) in view of McCaman et al. (J. Biol. Chem. 261:15345-15348). We respectfully disagree with the Examiner as claim 8 depends from claim 7 which depends from claim 1. For the reasons stated above, claim 1 is patentable over Moloney. The deficiencies in Moloney are not remedied by McCaman which merely teaches that the zymogen form of chymosin is activated at pH 2 to form a pseudochymosin product that is further processed to chymosin at pH 4.5. Applicant is not attempting to claim the activation conditions of chymosin.

5. The Examiner has objected to claim 27 under 35 U.S.C §103(a) as being unpatentable over Moloney (WO 96/21029) in view of Fine et al. (Gen Comp Endocrinol 89:51-61). We respectfully disagree with the Examiner for the reasons that follow.

Claim 27 depends from claim 26 which depends from claim 20. Claim 20 is patentable over Moloney for the reasons stated above. The deficiencies in Moloney are not remedied by Fine et al. Fine et al. teach the nucleic sequence of carp growth hormone. Fine et al. do not teach or suggest a chymosin pro-peptide-hirudin fusion protein.

In view of the foregoing, we respectfully request that the objections to the claims under 35 U.S.C. §103 be withdrawn.

The Commissioner is hereby authorized to charge any deficiency in fee or credit any overpayment to our Deposit Account No. 02-2095.

Attached hereto is a marked-up version of the changes made to the claims by the current amendment. The attached page is captioned "Version with markings to show changes made".

In view of the foregoing, we submit that the application is in order for allowance and an early indication to that effect would be greatly appreciated. Should the Examiner like to discuss the matter, he is kindly requested to contact Micheline Gravelle at 416-957-1682 at his convenience.

Respectfully submitted,

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Claims:

Claims 1, 4, 6, 13, 20, 23, 25, 41, 42 and 44 have been amended as follows.

1. (Thrice Amended) A method for the preparation of a recombinant polypeptide comprising

a) transforming a host cell with an expression vector comprising:

(1) a nucleic acid sequence capable of regulating transcription in a host cell, operatively linked to

(2) a chimeric nucleic acid sequence encoding a fusion protein, the chimeric nucleic acid sequence comprising (a) a nucleic acid sequence encoding a pro-peptide [derived] from an autocatalytically maturing [zymogen] aspartic protease, linked in reading frame to (b) a nucleic acid sequence heterologous to the pro-peptide and encoding the recombinant polypeptide, wherein the heterologous nucleic acid sequence is located immediately downstream of the nucleic acid sequence encoding the pro-peptide; operatively linked to

(3) a nucleic acid sequence encoding a termination region functional in said host cell,

b) growing the host cell to produce said fusion protein; and

c) adding a mature form of an autocatalytically maturing zymogen to the fusion protein so that the pro-peptide is cleaved from the fusion protein to release the recombinant polypeptide.

4. (Twice Amended) A method according to claim 1 wherein said [pro-peptide is derived from a zymogen] aspartic protease is selected from the group consisting of

chymosin, [trypsinogen,] pepsin, HIV-1 protease, pepsinogen, cathepsin and yeast proteinase A.

6. (Amended) The method according to claim 1 wherein the chimeric nucleic acid sequence does not include a sequence encoding a mature form of the [zymogen] aspartic protease.

13. (Twice Amended) A method according to claim 1 wherein the mature form of the autocatalytically maturing zymogen added in step (c) is [homologous to the pro-peptide] an aspartic protease.

20. (Amended) A chimeric nucleic acid sequence encoding a fusion protein comprising (a) a nucleic acid sequence encoding a pro-peptide from an autocatalytically maturing [zymogen] aspartic protease and (b) a nucleic acid sequence encoding a polypeptide that is heterologous to the pro-peptide.

23. (Amended) A chimeric nucleic acid sequence according to claim 20 wherein the [pro-peptide is derived from] aspartic protease is chymosin, [trypsinogen,] pepsin, HIV-1 protease, pepsinogen, cathepsin or yeast proteinase A.

25. (Amended) A chimeric nucleic acid sequence according to claim 20 which does not include a sequence encoding a mature form of the [zymogen] aspartic protease.

41. (Amended) A [pharmaceutical] composition comprising a chimeric nucleic acid sequence encoding a fusion protein, the chimeric nucleic acid sequence comprising (a) a first nucleic acid sequence encoding a pro-peptide [derived] from an

autocatalytically maturing [zymogen] aspartic protease and (b) a second nucleic acid sequence encoding a polypeptide that is heterologous to the pro-peptide.

42. (Amended) A food composition comprising a chimeric nucleic acid sequence encoding a fusion protein, the chimeric nucleic acid sequence comprising (a) a first nucleic acid sequence encoding a pro-peptide [derived] from an autocatalytically maturing [zymogen] aspartic protease and (b) a second nucleic acid sequence encoding a polypeptide that is heterologous to the pro-peptide.

44. (Amended) A composition according to claim 41 wherein said chimeric nucleic acid sequence does not include a sequence encoding a mature form of the [zymogen] aspartic protease.

Claims 2, 3, 21 and 22 have been deleted.